

U.S. Application No. 09/196,673  
Filed: November 20, 1998

Attorney Docket No. 05569.0004.CNUS03

### AMENDMENTS TO THE CLAIMS

Claims 1-44 - Canceled.

45. (Previously presented) A method according to claim 145 wherein said enzyme or fragment is at least 200 amino acids.
46. (Previously presented) A method according to claim 145 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
47. (Previously presented) A method according to claim 45 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
48. (Previously presented) A method according to claim 145 wherein particles formed by said expression are selected or screened to provide an individual displayed polypeptide specific binding pair member or a mixed population of displayed polypeptide specific binding pair members associated in respective particles with nucleic acid encoding said displayed polypeptide specific binding pair member or specific binding pair members, the specific binding pair member or specific binding pair members thus provided having ability to bind a complementary ligand.
49. (Previously presented) A method according to claim 48 wherein the particles are selected by affinity with a complementary ligand.
50. (Previously presented) A method according to claim 49 which comprises recovering any particles bound to said complementary ligand by washing with an eluant.
51. (Previously presented) A method according to claim 50 wherein the eluant contains a molecule which competes with said particles for binding to said complementary ligand.
52. (Previously presented) A method according to claim 49 wherein the particles are applied to said complementary ligand in the presence of a molecule which competes with said particles for binding to said complementary ligand.
53. (Previously presented) A method according to claim 48 wherein the particles are selected by enzymatic activity of the displayed polypeptide.
54. (Previously presented) A method of producing a specific binding pair member, the method comprising:
  - (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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55. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
56. (Previously presented) A method of producing a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
57. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
58. (Previously presented) A method of producing a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
59. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
60. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

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(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

61. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 60, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
62. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:  
(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
63. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 62, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
64. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

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(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

65. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 64, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.

Claims 66-77 – Canceled.

78. (Currently Amended) A method of producing a member of a specific binding pair, the method comprising:  
contacting a library of filamentous bacteriophage particles with a desired ligand, wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme, has enzymatic activity when displayed at the surface of filamentous bacteriophage particles, as measured in an enzymatic assay, and is at least 100 amino acids,  
wherein said filamentous bacteriophage particles display a population of specific binding pair members, and  
separating particles displaying specific binding pair members which bind to said desired ligand.
79. (Previously presented) A method according to claim 78 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.

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80. (Currently Amended) A method of producing a member of a specific binding pair, the method comprising:
- contacting a library of filamentous bacteriophage particles with a desired ligand, wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including said nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme, has enzymatic activity when displayed at the surface of filamentous bacteriophage particles, as measured in an enzymatic assay, and is at least 100 amino acids,
  - wherein said filamentous bacteriophage particles display a population of specific binding pair members, and
  - separating particles displaying specific binding pair members which have a desired enzymatic activity.
81. (Previously presented) A method according to claim 80 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
82. (Currently Amended) A method of producing a member of a specific binding pair, the method comprising:
- contacting a library of filamentous bacteriophage particles with a desired ligand, wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein which said enzyme or fragment thereof is able to bind a ligand of said enzyme, has enzymatic activity when displayed at the surface of filamentous bacteriophage particles, and is at least 200 amino acids,
  - wherein said filamentous bacteriophage particles display a population of specific binding pair members, and

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separating particles displaying specific binding pair members which bind to said desired ligand.

83. (Previously presented) A method according to claim 82 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
84. (Currently Amended) A method of producing a member of a specific binding pair, the method comprising: contacting a library of filamentous bacteriophage particles with a desired ligand, wherein said filamentous bacteriophage particles display on their surface a polypeptide which is a specific binding pair member capable of binding a complementary ligand, and each filamentous bacteriophage particle contains genetic material including nucleic acid encoding said polypeptide, which nucleic acid encoding the polypeptide is provided by mutation of nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which said enzyme or fragment thereof is able to bind a ligand of said enzyme, has enzymatic activity when displayed at the surface of filamentous bacteriophage particles as measured in an enzymatic assay and is at least 200 amino acids,
- wherein said filamentous bacteriophage particles display a population of specific binding pair members, and
- separating particles displaying specific binding pair members which have a desired enzymatic activity.
85. (Previously presented) A method according to claim 84 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
86. (Previously presented) A method of producing a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
87. (Previously presented) A method according to claim 86 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
88. (Previously presented) A method of producing a specific binding pair member, the method comprising:

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- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
- 89. (Previously presented) A method according to claim 88 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
- 90. (Previously added) A method of producing a specific binding pair member, the method comprising:
  - (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
- 91. (Previously presented) A method according to claim 90 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
- 92. (Previously presented) A method of producing a specific binding pair member, the method comprising:
  - (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
  - (ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.
- 93. (Previously presented) A method according to claim 92 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
- 94. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
  - (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
- 95. (Previously presented) A method according to claim 94 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
- 96. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

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- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
97. (Previously presented) A method according to claim 96 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
98. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
99. (Previously presented) A method according to claim 98 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
100. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and
  - (ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.
101. (Previously presented) A method according to claim 100 wherein said polypeptide is displayed as a fusion with a gene III capsid protein surface component of phage fd or its counterpart in another filamentous phage.
102. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:
- (i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and
  - (ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).



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103. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 102, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
104. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:  
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
105. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 104, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
106. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:  
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

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107. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 106, wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.
108. (Previously presented) A method of producing nucleic acid encoding a specific binding pair member, the method comprising:  
(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and  
(ii) producing from the nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member in a functional form comprising a binding domain for its complementary specific binding pair member, wherein said derivative specific binding pair member is produced by addition, deletion, substitution or insertion of one or more amino acids, or by linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).
109. (Previously presented) A method of producing a specific binding pair member, the method comprising:  
producing said derivative specific binding pair member by expression of nucleic acid produced according to the method of claim 108 wherein said derivative specific binding pair member is in a functional form comprising a binding domain for a complementary specific binding pair member.

Claims 110-144 – Cancelled.

145. (Currently Amended) A method of producing a specific binding pair member, which method comprises:  
expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides, which library of nucleic acid sequences is provided by mutating nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof wherein said enzyme or fragment thereof is a non-immunoglobulin protein, which enzyme or fragment thereof is able to bind a ligand of said enzyme, has enzymatic activity when displayed at the surface of filamentous bacteriophage particles, as measured in an enzymatic assay, and is at least 100 amino acids,

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wherein said polypeptides encoded by the library are displayed at the surface of filamentous bacteriophage particles, and wherein genetic material of each filamentous bacteriophage particle displaying a polypeptide includes nucleic acid encoding the polypeptide displayed on that particle.